Editorials

Hyperventilation disorders

Hyperventilation syndrome falls into the shadowy hinterland between physiology, psychiatry, psychology and medicine. In this respect it joins a long list of syndromes from the past of which effort syndrome is just one example. Myalgic encephalomyelitis (ME) and postviral fatigue syndrome are recent attempts to impose a unitary definition on what is probably a complex interaction between many different organic and psychological factors. The recent introduction of terms such as somatization disorder recognize this aetiological heterogeneity[1].

The symptoms of hypocapnia induced by voluntary overbreathing were first described by Haldane in 1908, the first case of spontaneous hyperventilation by Goldman in 1922[2], and the term Hyperventilation Syndrome was first used by Dalton, Kerr and Gliebe in 1937 to describe patients with symptoms both of hypocapnia and anxiety[3]. Since then, many different interpretations of this term have appeared in the literature encompassing patients with widely different aetiologies. Much research in this area is bedevilled by failure to define clearly the detailed characteristics of the patients studied; by the assumption of definitions for which there is no universal agreement; and by the presentation of scientifically unsound data lacking in rigorous quantitative proof and with perpetuation of circular arguments. The papers in this issue of the journal make a commendable attempt to reintroduce the reader to the historical perspectives of this subject and to clarify some of the issues, but unfortunately also have some of the shortcomings common to so many of the studies in this very difficult field.

Part of the difficulty with this disorder lies in lack of a gold standard for diagnosis[4]. Furthermore, there is often lack of common understanding between psychologists, therapists, physicians and physiologists, as well as failure to distinguish clearly between the rigorous requirements for a research paper and the more pragmatic requirements of everyday practice. Reviewing this field fairly is difficult and is bound to be biased towards the interests of the reviewer, in the present case towards the approach of a physiologist and chest physician.

To a clinician, it would seem that the easiest way to simplify this morass both for research and clinical purposes is to regard hyperventilation as a pathophysiological process which can be acute or chronic, and at least for the moment to avoid the use of the term 'Hyperventilation Syndrome' altogether. The physiological definition of hyperventilation is breathing in excess of metabolic requirements (ie CO_2 production) and by definition this implies arterial hypocapnia and an abnormally high drive to breathe. This increased drive inevitably has one or more causes which can be sought and listed. These causes can be of psychological, organic or physiological origin. Apart from florid and easily diagnosable causes of hyperventilation such as diabetic ketoacidosis, there are many causes of respiratory stimulation leading to hypocapnia which may not be immediately obvious. Anxiety, a key component in the original definition of hyperventilation syndrome, can undoubtedly cause hyperventilation as can depression[5] but may be absent, or if present may be secondary to the unpleasant symptoms of hypocapnia. Many organic diseases can cause excessive respiratory drive and profound hypocapnia with documented evidence in asthma[6], chronic bronchitis, emphysema, heart failure, chronic pain[7] and pulmonary embolus[8]. In asthma, hypocapnia is maximal with mild or moderate bronchoconstriction and in these mild cases classical asthmatic symptoms can be absent or almost unrecognizable.

There are a number of factors that may perpetuate hyperventilation. Apart from renal compensation, there appear to be physiological mechanisms resetting the P_{CO_2} to a lower level independent of chemoreceptor resetting[9,10]. Habit has been proposed as a perpetuating mechanism[11], and undoubtedly some subjects deliberately take large breaths in an attempt to relieve chest discomfort. Misattribution of symptoms of hypocapnia or, for example, mild asthma to serious disease[12] can also perpetuate hyperventilation.

The interaction of factors contributing to chronic hyperventilation remains uncertain. One possible scenario is that an acute episode of hyperventilation, with or without psychiatric disorder, leads to symptoms which are misdiagnosed or incorrectly diagnosed. As a consequence, the patient's anxieties are increased and further consultation sought. Thus the disorder is perpetuated and the patient is put at risk of becoming a chronic invalid[13]. Many 'doctor shoppers' may begin their careers with an episode of hyperventilation-related symptoms in this way. There are, however, as many models as there are research workers in this field and providing hard proof for these models is very difficult.

At a practical level, it is my view as a physician that, apart from the uncertainties about diagnosis and definition discussed above, imposing the label of 'hyperventilation syndrome' or 'effort syndrome' on the patient often distracts from a search for the causes of the hyperventilation, many of which, eg mild asthma, are eminently treatable. Regarding hyperventilation as a pathophysiological process rather than a disease per se simplifies the clinical management of these patients to a logical sequence of steps: (1) determine whether symptoms are or might be related to hypocapnia; (2) attempt to prove presence of continuous or intermittent hypocapnia or hyperventilation; (3) seek the causes of hyperventilation; (4) treatment.

To a physiologist, it would seem logical that hyperventilation should not be diagnosed without a clear demonstration of arterial or end-tidal hypocapnia. However, there are problems with this approach, the first of which concerns the normal range of arterial

0141-0768/90
120755-03/$02.00/0

or end-tidal P_{CO_2}. In our laboratory, we use a value of 30 mmHg as the lower limit[9,10], but this should ideally be standardized for each laboratory and can be profoundly affected by the total physiological inputs to respiration and the conscious state of the subject. In early papers in this field, measurement of P_{CO_2} was tedious, difficult and rarely attempted. Even in recent papers, measurement of P_{CO_2} is often not attempted because of the perceived intermittent nature of the hyperventilation and the lack of technology for long-term ambulatory measurement of arterial or end-tidal P_{CO_2}. Recent attempts to use the transcutaneous electrode have been dogged by the unacceptably slow time constant of this electrode making interpretation of the results difficult[14]. Despite these methodological problems however, such research that has been published using these electrodes for ambulatory measurement has important implications and can be summarized as follows: (1) some but not all patients hyperventilate during panics; (2) the hyperventilation provocation test has many shortcomings; (3) there is no association between the absolute levels of P_{CO_2} and the nature of symptoms reported; and (4) breathing retraining is of no specific benefit to patients identified as 'hyperventilators' by a provocation test; it may merely have a non-specific effect in anxious patients[15].

End-tidal measurements via a catheter inserted a few millimeters into a nostril can give reliable measurements of P_{CO_2}. We have employed a screening test for some years now performed by our lung function technicians in which Pet CO_2 is measured over an extended period at rest and in response to a variety of stressors[10]. Such a test will detect both chronic hypocapnia and a tendency to hypocapnia but cannot prove that symptoms experienced outside the laboratory were necessarily related to hypocapnia. In my opinion, this disorder will only gain recognition by mainline physicians and physiologists when scientific papers in the field use excessively rigorous criteria for definition and diagnosis. This means that demonstration of hypocapnia should have a high priority.

Symptoms are also unsatisfactory as a basis for diagnosis[16,17]. As illustrated in the papers in today's issue, the symptoms of hypocapnia are very vague and non specific, only tetany being truly specific to hypocapnia. 'Air hunger' or difficulty inspiring is suggestive[9]. Chest pain can be severe and can often be mistaken for coronary ischaemia but the cause of this is uncertain. Hyperventilation can certainly cause false positive changes in the ECG during a cardiac exercise study[18,19]. Reproduction of reported complaints by voluntary over-breathing, although useful for diagnosis and treatment, has already been discredited as an adequate criterion for the diagnosis of hyperventilation for research purposes[20].

Signs are equally unsatisfactory. Because of the shape of the relationship between CO_2 production, alveolar ventilation and P_{CO_2}, the latter can fall to low levels with only a small increase in ventilation[9,10,13] and this increase becomes slower with acclimatization. Thus severe chronic hyperventilation can be present with virtually undetectable increase in chest wall movements; if detectable, either panting or sighing can predominate. Gross panting is not necessarily associated with hypocapnia if the volume of each breath is sufficiently small to fail to clear the dead space.

How the term 'hyperventilation syndrome' could be made to fit in with this scheme is uncertain. In our chronic patient group, formal psychiatric morbidity was absent in 50% making a diagnosis of classic hyperventilation difficult. We preferred the descriptive term 'chronic hyperventilation of unknown aetiology' for these patients, avoiding the use of a label[9,10]. Undoubtedly, a subgroup of these would satisfy criteria for somatization disorder[1].

Without an agreed diagnostic process or even an agreed definition for this disorder it is almost impossible to carry out proper treatment studies. Explanation, reassurance and relaxation may have a role but controlled studies are lacking. Recent evidence from controlled studies suggests that breathing retraining has limited effectiveness[21]. Drugs appear to have only minimal long-term benefit.

The state of diagnosis and definition of hyperventilation-related disorders is therefore in considerable disarray which the papers in the present issue attempt to clarify with only partial success. It is unfortunate that others have not yet validated the usefulness of the 'think test', which is one of a number of provocation tests designed to unmask a tendency to hyperventilate when the resting P_{CO_2} is normal. The worry with this test is whether it can be universally applied, or whether its usefulness depends on the behaviour of the operator. There is also no agreement as to whether patients who are positive on this test could be regarded as having the 'hyperventilation syndrome' or merely a heightened susceptibility to hyperventilation which could be due to many different abnormal respiratory drives.

How myalgic encephalomyelitis and chronic fatigue overlap with hyperventilation is also uncertain. It could be argued that the history of ME is more exemplified by the case of neurasthenia than that of effort syndrome[22] although all three disorders are related. Nixon and colleagues (this issue, pp 761 and 765) should, however, be commended for seeking an explanation for this disorder not based on blind acceptance of the 'virus in the muscle' theory. However, in seeking to ascribe it all to hyperventilation they espouse a unitary explanation that runs counter to all the recent evidence[23,24]. There is incontrovertible evidence that the most significant feature of ME or chronic fatigue states is their association with affective disorder[25,26]. The paper could also be criticised for the criteria for defining hyperventilation, the absence of criteria for patient selection, and for ignoring the effect of 'effort after meaning' and recall bias in the retrospective accounts given by these exhausted and demoralized patients.

William Gardner
Department of Thoracic Medicine
King's College School of Medicine and Dentistry
Bessemer Road, London SE5 9PJ

References

1 Bass CM, Murphy MR. Somatisation disorder: critique of the concept and suggestions for future research. In: Bass C, ed. *Somatisation: physical symptoms and psychological illness*. Oxford: Blackwells, 1990
2 Goldman A. Clinical tetany be forced respiration. *JAMA* 1922;78:1193-5
3 Kerr WJ, Gliebe PA, Dalton JW. Physical phenomena associated with anxiety states: the hyperventilation syndrome. *California & Western Medicine* 1938;48: 12-16

4 Lewis RA, Howell JBL. Definition of the hyperventilation syndrome. *Bull Eur Physiopathol Respir* 1986;**22**: 201-5
5 Damas Mora J, Grant L, Kenyon P, Patel MK, Jenner FA. Respiratory ventilation and carbon dioxide levels in syndromes of depression. *Br J Psychiatry* 1976;**129**:457-64
6 McFadden ER Jr, Lyons HA. Arterial blood gas tensions in asthma. *N Engl J Med* 1968;**278**:1027-32
7 Glynn CJ, Lloyd JW, Folkhard S. Ventilatory response to intractable pain. *Pain* 1981;**11**:201-11
8 Szucs MM, Brooks HL, Grossman W, *et al.* Diagnostic sensitivity of laboratory findings in acute pulmonary embolus. *Ann Intern Med* 1971;**74**:161
9 Bass C, Gardner WN. Respiratory and psychiatric abnormalities in chronic symptomatic hyperventilation. *BMJ* 1985;**290**:1387-90
10 Gardner WN, Meah MS, Bass C. Controlled study of respiratory responses during prolonged measurement in patients with chronic hyperventilation. *Lancet* 1986;ii:826-30
11 Lum LC. The syndrome of habitual chronic hyperventilation. *Recent Adv Psychosomatic Med* 1976; 3:196-230
12 Salkovskis PM, Clark DM. Cognitive and physiological processes in the maintenance and treatment of panic attacks. In: Hand I, Wittchen H-V, eds. *Panic and phobias*, Heidelberg: Springer, 1986
13 Gardner WN, Bass C. Hyperventilation in clinical practice. *Br J Hosp Med* 1989;**41**:73-81
14 Pilsbury D, Hibbert G. An ambulatory system for long term continuous monitoring of transcutaneous PCO2. *Bull Eur Physiopathol Resp* 1987;**23**:9-13
15 Hibbert G, Pilsbury D. Hyperventilation: is it a cause of panic attacks? *Br J Psychiatry* 1989;**155**:805-9
16 Grossman P, de Swart JCG. Diagnosis of hyperventilation syndrome on the basis of reported complaints. *J Psychosom Res* 1984;**28**:97-104
17 Stoop A, de Boo T, Lemmens W, Folgering H. Hyperventilation syndrome: measurement of objective symptoms and subjective complaints. *Respiration* 1986; **49**:37-44
18 Chambers JB, Kiff PJ, Gardner WN, Jackson G, Bass C. Value of measuring end tidal partial pressure of carbon dioxide as an adjunct to treadmill exercise testing. *BMJ* 1988;**296**:1281-5
19 Bass C, Chambers JB, Kiff P, Cooper D. Panic anxiety and hyperventilation in patients with chest pain: a controlled study. *Q J Med* 1988;**69**:949-59
20 Wientjes C, Grossman P, Defares P. Psychosomatic symptoms, anxiety and hyperventilation in normal subjects. *Bull Eur Physiopathol Resp* 1984;**20**:90-1
21 De Reuter C, Rijken H, Garssen B, Kraaimaat F. Breathing retraining, exposure and a combination of both, in the treatment of panic disorder and agoraphobia. *Behav Res Ther* 1989;**27**:647-55
22 Wessley S. 'Old wine in new bottles': neurasthenia and 'ME'. *Psychol Med* 1990;**20**:35-53
23 David A, Wessley S, Pelosi A. Post-viral fatigue: time for a new approach. *BMJ* 1988;**296**:696-99
24 Swartz M. The chronic fatigue syndrome - one entity or many. *N Engl J Med* 1988;**319**:1726-8
25 Wessley S, Powell R. Fatigue syndromes: a comparison of chronic 'postviral' fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg Psychiatry* 1989;**52**:940-48
26 Gold D, Bowden R, Sixbey J, Riggs R, Katon WJ, Ashley R, Obrigewitch R, Corey L. Chronic fatigue. A prospective clinical and virological study. *JAMA* 1990;**264**:48-53

Homo sapiens - a species too successful

The development, mental and otherwise, of our species, despite its failure to include the ability which many species have, of being able to consume and utilize hypertonic aqueous solutions of salt and to digest albeit indirectly many insoluble carbohydrates such as cellulose, has led to it being very much more adaptable to living and reproducing in all the kinds of conditions encountered on this planet than any other species. In terms of nutrition, the fact of it being an omnivore has also been most helpful.

This superiority has led, during the last 10 or more millennia to a remarkable ascendancy over the rest of the animal and vegetable world in which the needs of man have been imposed on the rest of the living organisms in the world. 'Lesser' living things have become designated as servants to or food for man, harvested or culled at will, and all controlled in number, habitat, breeding and development by man. Furthermore, man by his skills particularly evidenced in the last 100-150 years, has potentially and factually largely overcome pestilence and famine, and war is at least in abeyance at present in any major manifestation. Together with all this has gone the ever-increasing rate of usage of the available minerals, fossil fuels, soil fertility, fresh water reserves and all the remaining past and current present earthly raw materials which are necessary in making up the incredibly complicated and sophisticated background to the present-day lives of *Homo sapiens* other than many of those in the Third World.

In addition to all of this, in most parts of the world mankind is still breeding prolifically, infant mortality has become relatively low, and longevity is much more commonplace largely because drugs and surgery have improved immeasurably. It is predicted that world population will double from the present circa 5.2 to 10 or 11 Bn during the next 30-40 years.

This species' success story is unique in the history of planet Earth, and in every individual state economy, particularly in the Western World, growth is the 'in' word. Growth in number of consumers, growth in amount consumed, growth in profits, growth in savings, growth in waste production, growth in just about everything. This growth philosophy, its qualified success so far but its likely implications in view of the finite nature of our environment - the planet Earth - needs very much more (and urgent) examination, because implicit in growth and including the growth of populations is the ever-increasing utilization and rate of utilization of a great number of both replaceable and irreplaceable elements in this finite environment.

Only one of these growth areas - all of which are of great concern - is for consideration here, the area of growth in food consumption and its likely outcome in the relatively near future. By this is not meant any involvement in the sophistication of modern nutritional science and practice, but in most basic

0141-0768/90
120757-03/$02.00/0